



# The **network** maker

Drug resistance poses significant potential problems in the fight against HIV and TB, but little is known about how best to tackle it. **Dr Tulio de Oliveira** heads a network that aims to fill this knowledge gap



**To begin, how did your interest in the origins of HIV and the effect of networks of transmission arise?**

My interest in the origins of HIV began during my PhD studies at the Nelson R Mandela

School of Medicine, University of KwaZulu-Natal (UKZN), South Africa. It increased further during an EC Marie Curie research fellowship in the Evolutionary Biology Group at Oxford University, UK. Together with colleagues at Oxford, we used evolutionary techniques to characterise the origin of a nosocomial HIV transmission network in Libya. The results were used as motivation to prove the innocence of six medical personnel condemned to death for infecting 438 children in Benghazi, Libya.

I am still very interested in how bioinformatics and evolutionary analysis can be used to shed light on HIV transmission. Recently we used DNA sequencing to identify the source of a surrogate transmission case in South Africa, while at present we are working with large datasets from the Southern African Treatment and Resistance Network (SATuRN) produced by the Wellcome Trust Africa Centre for Health and Population Studies to characterise factors associated with HIV transmission in generalised epidemics in a hyperendemic HIV and tuberculosis (TB) area of rural South Africa.

**What are some of SATuRN's main activities?**

The mission of SATuRN is to build collaborations between researchers, clinicians and policy makers to address some of the key issues related to the delivery of antiretroviral and anti-TB therapy in Africa. In particular, the network's focus is on building an integrated response to the threat of drug resistance through the use of low-cost genotypic resistance testing and open source databases for patient management, public health surveillance and scientific research.

We have now implemented models of drug resistance testing and treatment failure management at several different levels in the region. Overall, we have more than 7,000 individual HIV resistance genotypes collated with clinical data, allowing real-time surveillance and providing powerful datasets for research. We have also trained over 1,500 healthcare workers and laboratory personnel from the region in the

diagnosis, management and prevention of drug resistance.

### Can you outline the main aims and objectives of the network?

Our vision is to build clinical, laboratory and research capacity to support the long-term response to the combined HIV/TB epidemic in Africa. SATuRN currently includes 24 research partners in southern Africa, in addition to collaborators from the US, Europe and South America. There is a blend of clinicians, public health professionals, laboratory scientists and bioinformaticians. This interdisciplinary mix helps to broaden the horizons of each individual partner and build consensus on the most important areas for scientific research. It also helps to make sure that scientific discovery can be translated into healthcare delivery and impact.

### Your annual drug resistance workshop is set to take place on 14-16 August this year. What will be some of the principal topics of discussion?

Our focus is always on distilling the latest science and discussing the implications for clinical practice. We expect results from national drug resistance surveys in South Africa for HIV and TB, and these are likely to inform discussion and debate around current treatment policies and also around the role of drug resistance testing within the public health response. We will also bring up-to-date information about developments in diagnostics and therapeutics, with several new TB drugs and antiretrovirals in the pipeline.

### Lastly, in response to the explosive HIV and TB epidemics in southern Africa, what do you see as the future for HIV treatment?

I think that the future will bring many challenges – the much vaunted 'end to AIDS' seems distant from where we are working. We are already seeing an increasingly complex case mix in the public health system and have even been managing patients with combined antiretroviral and anti-TB drug resistance. A public health approach to the delivery of HIV and TB treatment becomes more challenging as the case mix becomes more complex, and particularly as drug resistance emerges to first- and second-line therapies. There is a real need to stay ahead of the game and make sure that we are discovering and developing better diagnostics, drugs and treatment strategies to sustain the response for the next 10-20 years.

## Breaking down resistance

Widely deployed, antiretroviral and anti-tuberculosis therapies are saving lives in southern Africa, but at the price of increasing drug resistance. An initiative by researchers at the **Wellcome Trust Africa Centre for Health and Population Studies**, University of KwaZulu-Natal in South Africa is showing success in bucking this trend

**SOUTHERN AFRICA REPRESENTS** one of the world's hotspots in the fight against HIV and tuberculosis (TB). With statistics indicating some of the highest percentages of prevalence on the planet, any impact made on the diseases' infection rate could produce a lasting legacy, improving the life expectancies of a large swathe of the population.

Recent efforts by the medical community have resulted in a wider distribution of HIV/AIDS antiretroviral (ART) and anti-TB therapy in an attempt to reduce the chances of further infection among the adult population and the transmission of the disease to newborn babies. In South Africa – one of the countries hardest hit by HIV and TB, with the highest patient burden in the world – the rapid expansion of the HIV and TB treatment programme has brought positive results. However, at the same time it has created a new set of problems researchers have to grapple with.

### RISK OF DRUG RESISTANCE

The massive scaling up of ART and anti-TB therapy has led to an increased risk of individuals developing drug resistance, a grave threat to the sustained achievements of this strategy. Drug resistance limits the impact of proven treatments, eventually reducing their effectiveness and slowing down containment of an infection. This situation is made worse by the lack of laboratory resources and trained personnel to set up a working drug resistance monitoring programme and assist patients who develop resistance.

Under the directorship of Dr Tulio de Oliveira from the Africa Centre for Health and Population Studies of the University of KwaZulu-Natal and Professor Christopher Seebregts from the South African Medical Research Council, the Southern African Treatment Resistance Network (SATuRN) aims to build capacity to support an effective response to the HIV epidemic over the long term, developing collaborations between active researchers, clinicians and policy makers, and focusing on the monitoring, evaluation and delivery of ART in Africa.

At the same time, SATuRN is centred on collecting, analysing and distributing data on drug resistance, having established two of the most detailed databases in the world on this crucial subject – the Stanford HIV Drug Resistance Database and the RegaDB Clinical Management and Drug resistance Database – in South Africa and Botswana.

### LOCAL PROBLEMS, REMOTE SOLUTIONS

To remove problems caused by lack of resources and personnel devoted to monitoring drug resistance, SATuRN gathered inspiration from the tenets of telemedicine, creating a network in which genotyping and interpretation roles are left to remote specialised physicians, sparing local centres the burden of recruiting these personnel or building the elaborate computer systems required to process the huge amounts of data on the subject. Several models of testing and treatment failure management have been introduced at



## INTELLIGENCE

### SOUTHERN AFRICAN TREATMENT RESEARCH NETWORK

#### OBJECTIVES

- To build innovative collaborations between researchers, clinicians and policy makers focused on the monitoring, evaluation and delivery of antiretroviral and anti-tuberculosis therapy in Africa
- To collect, curate, interpret and disseminate sequence and drug resistance data
- To increase access to efficient, lower cost genotyping and drug resistance testing in Africa
- To expand clinical and laboratory training to build research capacity and enhance treatment throughout Africa

#### KEY COLLABORATORS

For a full list of collaborators and partners, please visit [www.bioafrica.net/saturn/saturnpartners.html](http://www.bioafrica.net/saturn/saturnpartners.html).

#### FUNDING

Council for Scientific and Industrial Research (CSIR) as part of the Swiss South African Joint Research Programme (SSJRP), South Africa and Switzerland • European Commission (EC), Belgium • Presidential Plan for AIDS Relief (PEPFAR), USA • US Center for Diseases Control (CDC), USA • Wellcome Trust, UK

#### CONTACT

**Dr Tulio de Oliveira**  
Director, SATuRN

Africa Centre for Health and Population Studies  
University of KwaZulu-Natal  
PO Box 198  
Mtubatuba  
KwaZulu-Natal 3935  
South Africa

T +27 35 550 7542  
E [tuliodna@gmail.com](mailto:tuliodna@gmail.com)  
E [tdeoliveira@afriacentre.ac.za](mailto:tdeoliveira@afriacentre.ac.za)

[www.bioafrica.net/saturn](http://www.bioafrica.net/saturn)

**DR TULIO DE OLIVEIRA** is a bioinformatician who has been conducting HIV research since 1997. After receiving his PhD from the Nelson R Mandela School of Medicine, University of KwaZulu-Natal (UKZN) he took a Marie Curie research fellowship at the University of Oxford, UK in 2004-06. He has published many high-impact articles including one that proved the innocence of six foreign medical personnel condemned to death for infecting 438 children with HIV in a hospital in Libya; the first case of proven HIV surrogate transmission in South Africa; and the first public HIV drug resistance database in Africa. He is currently a senior researcher at the Wellcome Trust Africa Centre for Health and Population Studies, UKZN and the Director of SATuRN.

different levels: at the individual programme level in KwaZulu-Natal; at province-wide level in the Free State; and even nationwide in Botswana, proving that the system can be applied on various scales.

This approach allows the expertise of leading centres and scientists to be applied in a capillary way, and at the same time allows the SATuRN consortium to gather an impressive amount of information for clinical surveys, filling the wide gaps in drug resistance data present at the moment.

#### AMAZING INFORMATION

SATuRN – which currently includes 24 partners in southern Africa – boasts a collection of over 7,000 resistance genotypes open to researchers and postgraduate students. Over the past few years, the network has grown to also include external experts, and there are plans to extend this successful model beyond the region currently covered, to develop added capacity in other HIV hotspots of the continent.

SATuRN's remit also extends beyond its original priority on HIV. Commonalities in the molecular mechanism of drug resistance have prompted attention to switch to the links between HIV and TB, and to the need of developing an integrated response to the two diseases. Collaboration with Dr Richard Lessells from the TB Centre of the London School of Hygiene and Tropical Medicine (LSHTM) saw the network gain an expanded capacity for TB research, and further shared initiatives are being planned.

#### CENTRALISED EXPERTISE

The threat of drug resistance is addressed via an integrated response focusing on low-cost genotypic resistance testing, for which the thousands of collated genotypes form a vital backbone. The key aspect of the project is to enable local physicians and practitioners, who have direct interaction with patients, to submit medical data of those they identify as not responding to treatment for processing at a remote facility. This approach, described by de Oliveira as a 'virtual treatment

failure clinic' allows local clinicians to request advanced diagnostic tests and specialist advice even from the most remote locations. In addition to providing potential lifesaving treatment information, a further benefit is the knowledge garnered by local nurses, who can become experts at spotting resistant subjects and can therefore play an increasingly important part in the process.

#### REDUCING COSTS

A traditional stumbling block for similar approaches in the past was the availability and expense of the testing kit necessary to produce the basic data for a diagnosis. The development and implementation of a cheaper resistance genotype test, a key objective for SATuRN, has been a real achievement in the last few years. A working cooperation was established with a network of government and academic laboratories, while a successful partnership with private firms – in this case, Life Technologies – saw SATuRN reduce the cost of this vital test by approximately half, allowing it to become available for a much larger number of potential patients. Despite this significant step, much remains to be done in this field and several areas need to be investigated in detail for innovative ways to drive costs down. However, these first results are surely encouraging and point towards the kit becoming increasingly available in resource-limited settings of southern Africa.

Through the cooperation of a wide consortium of scientists, policy makers and informaticians, the SATuRN project is a poster model for the powerful role of integration in the development and delivery of cheaper and better diagnostic tools – and a model that is ready to be applied to an even wider range of situations. While the future will surely present researchers and clinicians with several new challenges, projects like SATuRN can provide the tools to face the emergence of new types of drug resistance that are currently posing dangers to the delivery of effective anti-HIV and anti-TB treatment.

The SATuRN project is a poster model for the powerful role of integration in the development and delivery of cheaper and better diagnostic tools



[bioafrica.net/saturn](http://bioafrica.net/saturn)